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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,164	11/09/1999	BENJAMIN EITHAN REUBINOFF	13164	6220

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GARDEN CITY, NY 11530

EXAMINER

WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 05/01/2003

24

Please find below and/or attached an Office communication concerning this application or proceeding.

SM

**Advisory Action**

Application No.  
**09/436,164**

Applicant(s)  
**Reubinoff, B. E.**

Examiner  
**Joseph Weitach**

Art Unit  
**1632**



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED Apr 21, 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

- a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see NOTE below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_

4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See attached.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_

Claim(s) objected to: \_\_\_\_\_

Claim(s) rejected: 20-26 and 38-44

Claim(s) withdrawn from consideration: 1-18, 29-36, 45, and 46

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_

10. ☒ Other: It is noted that nonelected claims were not canceled as required in response to the final office action (paper 22, page 3).

*Deborah Crouch*  
**DEBORAH CROUCH**  
**PRIMARY EXAMINER**  
**GROUP 1800 1630**

Art Unit: 1632

Section 5(c):

Applicants summarize the teaching of the Thomson *et al.* references and the basis of the rejection. In particular, Applicants note that Thomson *et al.* only teach spontaneous differentiation not the specific induction of differentiation. Applicants argue that the specification provides culture conditions which induce differentiation (page 20, lines 23-25) and that these conditions are recited in the claims. Finally, Applicants argue that the present inventor uniquely recognized that various batches of fibroblast cells differed in their potential to support ES cell growth and differentiation in culture. Applicants' arguments have been fully considered, but not found persuasive.

First, it is noted that the instant claims encompass the conditions for the spontaneous differentiation of ES cells taught by Thomson *et al.* In particular, the specification teaches that a variety of conditions can be used to induce differentiation including "cultivating to a high density in monolayer" (page 22, lines 6-8) which is the same condition inducing differentiation in Thomson *et al.* Further, Examiner notes that the specification teaches that conditions such as period in culture, density and feeder layer can affect deaffectation of the cells in culture (page 20), however Thomson *et al.* also teaches that time between passage and density are important factors in culturing ES cells, in particular with respect to their affect on differentiating the ES cells in culture. With respect to the role of the fibroblast feeder cell layer, clearly Thomson *et al.* teach that a fibroblast feeder layer is required to prevent differentiation of human ES cells. Further, Thomson *et al.* teaches that under the appropriate conditions ES cells can be induced to

Art Unit: 1632

differentiate on a fibroblast feeder layer. The present claims are broad encompassing the methods of maintaining and differentiating ES cells taught by Thomson *et al.* It may be, as Applicants argue, that various specific fibroblast cells lines provide a more or less favorable substrate to maintain embryonic stem cells, however the instant claims are very broad and even dependent claims are not restricted to any particular fibroblast cell line or that the fibroblast feeder cells provide any specific differentiation affect. Further, while the handling or the source of fibroblast cell may affect its suitability to serve as a feeder layer, there is no objective evidence of record that the fibroblast layer itself uniquely affects ES cells differentiation, and that other conditions such as growth at high density or the addition of differentiation factors to the media are required for differentiation. It is noted that Applicants describe two different feeder cell lines, B-83 and B-72 (amendment, pages 7-8), however these are not presented in the specification nor is there any specific data to evaluate the nature of these cells or the conditions of culture which provided the affect described in Applicants' comments. The instant claims encompass any culturing condition which induce any type of differentiation of the ES cells. Thomson *et al.* teach the same method of isolating embryonic stem cells as recited in the claims and provide specific conditions in which the ES cells differentiated in culture. Given the breadth of the instant claims, the teaching of Thomson *et al.* anticipate the claimed invention.